Electronic Supplementary Information for Dalton Transactions

In vitro studies of 3-hydroxy-4-pyridinones and their glycosylated derivatives as potential agents for Alzheimer's disease

David E. Green,[†] Meryn L. Bowen, [†] Lauren E. Scott, [†] Tim Storr,[†] Michael Merkel,[†] Karin Böhmerle,[†] Katherine H. Thompson,[†] Brian O. Patrick,[†] Harvey J. Schugar,[‡] and Chris Orvig.[†,*]

†Medicinal Inorganic Chemistry Group, Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, BC, V6T 1Z1, Canada;
‡ Department of Chemistry and Chemical Biology, Rutgers, The State University of New Jersey, 610 Taylor Rd, Piscataway, New Jersey 08854-8087, USA.
**Author to whom correspondence should be addressed; e-mail orvig@chem.ubc.ca, Ph 1 604 822 4449.*

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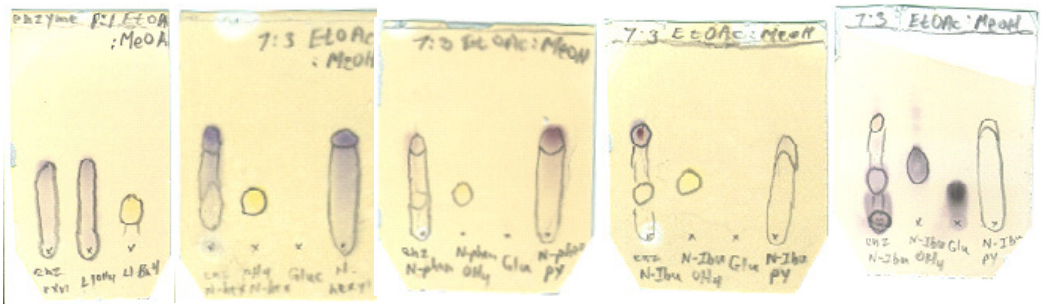

E 2b 2d E 3d G 3b E 4d G 4b E 5d G 5b E 5d G 5b

Figure S1 Silica TLC monitoring of Abg enzyme reactions with pyridinone glycosides. E = enzyme reaction with Abg added to initiate the reaction; G = Glucose. TLCs were run after reacting ~30 min. Spots that were UV-active (254 nm lamp) are outlined. The highest R_f spots correspond to the free pyridinones that turn purple-blue in colour with $FeCl_3$ spray. Glucose is only visualized after charring (not at 254 nm). The starting pyridinone glycosides have a lower R_f than the free pyridinones and turn pale yellow in colour with $FeCl_3$ spray. A representative acid charred TLC plate is also shown (v).

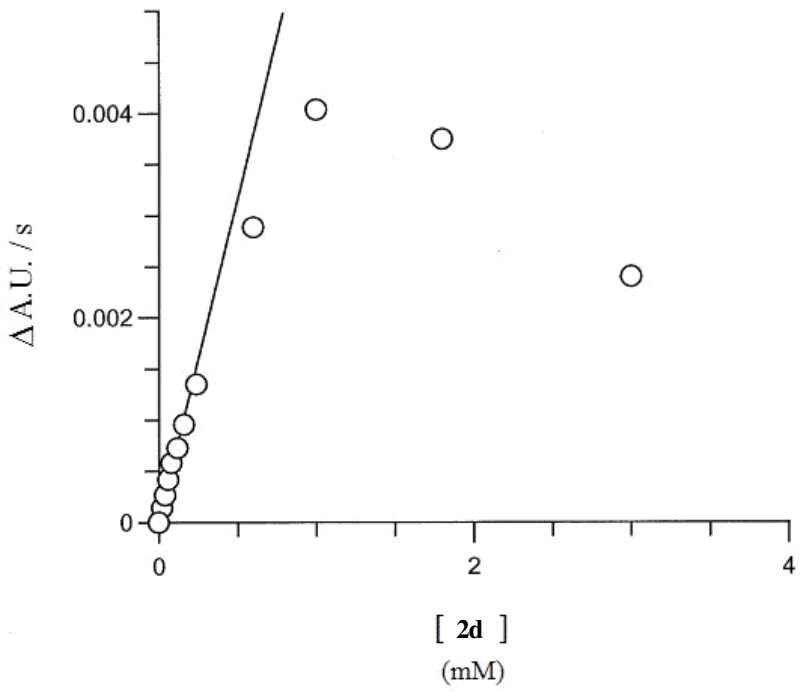

Figure S2 Initial rates versus substrate concentrations for **2d** and Abg in sodium phosphate buffer at 37°C. The initial slope for lower substrate concentrations was determined to be 0.00628 ± 0.00040 using GraFit. From the initial slope, k_{cat}/K_m was calculated to be 12.2 ± 0.8 $s^{-1}mM^{-1}$.

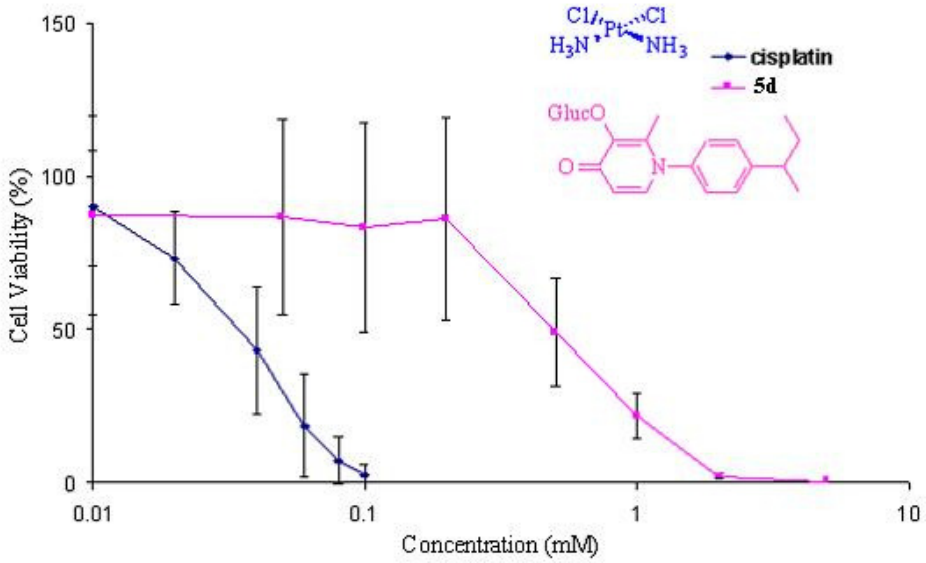

Figure S3 MTT plots for **5d** and cisplatin, with IC_{50} values equal to 570 ± 90 and 35 ± 5 μM, respectively. The error bars indicate one standard deviation of the averaged cell percent viability. Error bars for each point represent ± 1 SD above and below the average. Cell viabilities for each concentration were done in sextuplicate (6 wells each).

Table S1 Selected crystallographic data for **2d** and **Cu(5b)$_2$**.

	2d	**Cu(5b)$_2$**
Empirical Formula	$C_{13}H_{19}NO_7$	$C_{36}H_{48}N_2O_6S_2Cu$
Formula Weight	301.29	732.42
Crystal Dimensions	0.50 X 0.25 X 0.10 mm	0.35 X 0.10 X 0.08 mm
Crystal System	Monoclinic	Monoclinic
Lattice Parameters	a = 8.2508(8) Å	a = 16.881(2) Å
	b = 8.0153(6) Å	b = 21.182(2) Å
	c = 11.633(1) Å	c = 10.6465(9) Å
	β = 113.797(4)°	β = 100.614(4) o
	V = 703.9(1) Å^3	V = 3741.8(7) Å3
Space Group	P2$_1$ (#4)	*P* 2$_1$/*c* (#14)
Z	2	4
Calculated Density	1.421 g/cm^3	1.300 g/cm3
Wavelength	0.71073 Å	0.71073 Å
μ	1.16 cm^{-1}	7.40 cm-1
T	253(1) K	253(1) K
*R*1(F$_o$)	0.048	0.075
*wR*2(F$_o^2$)	0.121	0.113

Table S2 TEAC values ± SD for 1, 3, and 6 minutes.

Compound	1 min	3 min	6 min
α-Toc	0.72 ± 0.02	0.72 ± 0.03	0.72 ± 0.03
BHT	0.13 ± 0.01	0.23 ± 0.01	0.34 ± 0.01
2b	0.67 ± 0.02	0.71 ± 0.02	0.74 ± 0.02
3b	0.73 ± 0.02	0.82 ± 0.02	0.83 ± 0.02
4b	0.82 ± 0.04	1.04 ± 0.04	1.12 ± 0.04
5b	0.82 ± 0.03	0.98 ± 0.03	1.05 ± 0.04
6b	1.10 ± 0.03	1.28 ± 0.04	1.34 ± 0.04

Table S3 Resolubilization efficiency of **2b** and **4b** compared to DTPA normalized to 100%.

Well contents	Zn^{2+} (pH 7.4)	Cu^{2+} (pH 6.6)
Aβ blank	93.3 ± 3.2	87.2 ± 5.3
Aβ+M	0.0 ± 12.9	0.0 ± 8.9
Aβ+M+ DTPA	100.0 ± 10.1	80.7 ± 5.0
Aβ+M+ **2b**	80.5 ± 3.0	77.6 ± 1.2
Aβ+M+ **4b**	40.0 ± 5.5	72.0 ± 2.7